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By A. S. Shevelev

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It is well known that it is comparatively easy to accomplish autotransplantation alone and, in part, isotransplantation of tissues. As a rule, homotransplants and heterotransplants slough off 10-12 days after grafting. In man, an exception is constituted by a homografting of cartilage and cornea; in the rat, of fascia, ovaries, and extremities (3,19).

The principal part in the sloughing-off process of transplants is played by the immunobiological mechanisms. The phenomenon of tissue incompatibility in grafting is primarily the result of antigenic differences between the donor and recipient tissues (4). These differences are shown most distinctly after the grafting is accomplished between different species (heterotransplantations). However, there are also antigenic differences between various individuals of the same species, which are manifested particularly in the existence of various blood groups; apart from the group specificity the existence of a type specificity is also been established associated with the

presence of "M" and "N" antigens in the erythrocytes (89). "A", "B", "M" and "N" antigens are found not only in erythrocytes but also in other cells of the organism (13, 14). Similar antigens exist not only in people but also in animals (30).

The fact that a second homo- or heterotransplant grafted a certain time after the first sloughs off much more quickly (8,9,25,26, 124, 141, 145) attests to the immunological basis of the phenomena of tissue incompatibility after grafting.

A number of research workers have established the existence of specific antibodies in the blood of the recipients on to whom transplants are grafted (6, 7, 8, 16). Specifically a study of agammaglobulinemia particularly attests to the role of antibodies into transplantation immunity. As is well known, this condition can be congenital or acquired and is characterized by the absence of a gamma-globulin fraction in the serum, and, therefore, also of antibodies which are usually localized in this fraction (32, 67,80). For the problem which we are taking up the fact is interesting that in these patients homotransplants "take" very well along with the absence of antibodies in the blood (68, 107, 140).

It has been established that rabbits can be sensitized to the skin of a donor by means of the administration of leucocytes obtained from this donor (108). Billingham, Brent, and Medawar (35, 36) have carried out a passive transference of the phenomenon of accelerated sloughing-off of a homotransplant

by means of the intraperitoneal administration of a suspension of cells obtained from regional lymph nodes and from the spleen of specifically sensitized donors into normal mice. Similar results have been obtained by Mitchison (115).

There are indications that the antigenic stimulus in the homoplastic grafting is associated with the neuclear substance and does not depend on the cytoplasm (38). Certain authors identify it with the desoxyribonucleoprotein (37), whereas others could not confirm this (78).

Lawrence (91) notes a similarity between the immunity to homotransplants and the tuberculin type of allergy.

Therefore, the data in the literature permit us to conclude that immunobiological mechanisms underlie tissue incompatibility in grafting. In connection with this, the problem arises as to the possibility of artificial suppression of transplantation immunity. Both specific and non-specific routes of depressing transplantation immunity are theoretically possible.

In this direction the study of the so-called "actively acquired immunological tolerance" is very promising. The basis of this study was constituted by the theoretical principles expressed by Burnet and Fenner (39) as well as by G.V. Lopashov and O.G. Stroyeva (18). These authors believed that animals do not react immunologically to a number of complexes of their own bodies because it grows at the same time as they do and, therefore, it /the body/ becomes tolerant of substances which under other conditions would manifest an

antigenic effect. From this standpoint substances which "mature" after the capacity for reacting immunologically has developed in the body, as a result of which the body cannot acquire a tolerance to their effect, are considered autoantigens, or else these are constituted by antigens which possibly manifest themselves early but cannot, under normal conditions, obtain access to territory where immunological reactions are developed. In the first category of autoantigens are the spermatozoa and, possibly, the proteins of milk; in the second category, the protein of lens and certain antigenic components of the brain.

Burnet and Fenner believe that if various antigens are introduced into the body during the embryonic period the immune system of the body will be able to adapt itself gradually to the given antigen, as a result of which a state of immunological tolerance can develop, that is, a resistance to this antigen in the post-embryonic period. The experimental research performed with the aim of checking these theoretical standpoints have confirmed these ideas (15, 24, 109, 110).

Among the other attempts at specifically suppressing the transplantation immunity mention may be made of the investigations of Csaba (53) on heterotransplantation of the spleen and the embryonic endocrine glands with the use of antiserum against organ specific antibodies as well as the works of Kaliss (86), who succeeded in increasing the success of tumor transplants in mice by means of the introduction of antiserum against the splenic tissue or donor tumor.

These facts attest to the possibility of increasing the degree of which transplants "take" as a result of a specific change in the immunobiological reactivity of the organism. However, the methods by means of which these data are obtained usually give very inconstant results. In addition, none of these methods permit the transplantation of any kind of tissue completely in experiments of home- and heterotransplantation.

In connection with this, the question arises whether this is possible at all. In other words: is it possible artificially to create chimaeras, that is, organisms in which the various tissues taken from an animal of another species not only would "take" completely but would also completely replace the morphologically and functionally corresponding recipient tissues?

From a theoretical aspect such a possibility can hardly be denied. It is natural to suppose that such chimaeras can be created in the event it is possible to suppress the congenital immunity of the recipient against antigens which are foreign to it. However, until recently attempts at accomplishing this have run up against insurmountable difficulties, associated chiefly with the fact that while it is possible to produce such a marked reduction in the natural immunity this usually leads to the death of the recipient.

New possibilities for accomplishing this problem have appeared in recent years in connection with the study of the biological effect of ionizing radiation, particularly in connection with the study of its effect on the immunological reactivity of the organism. At the present time, it has been

established that irradiation with moderate and large doses of ionizing radiation can produce a marked reduction in the natural immunity against a number of pathogenic and conditionally pathogenic microorganisms which, to a certain degree, is associated with a marked depression of the elaboration of antibodies in radiation injury. (10-12, 20-22, 27, 134 and others).

In addition, it has been shown that in radiation sickness a marked reduction in the congenital immunity is observed also with respect to foreign tissues of multicellular organisms (1, 2, 31, 122, etc.). However, the duration of this state is comparatively small, about three to four weeks, rarely longer. With the expiration of this period immunological reactivity of the organism, as a rule, is restored to normal, and the transplants slough off.

How can we surmount this difficulty?

New experimental possibilities in this direction have appeared with the study of a problem which, it would appear, has no direct connection with this matter. We are referring to the treatment of radiation sickness by means of the administration of a cellular suspension of hematopoietic tissue. It has been established that screening of the spleen with lead during a total-body X-irradiation as well as the intravenous administration of a splenic suspension from a non-irradiated donor immediately after the irradiation exert a considerable effect in radiation sickness. These results were obtained by Jacobson and others (82-84) and have been confirmed by other research workers (40-46, 90, 64, 117 and others).

An even more pronounced protective effect has been obtained from the intravenous administration of a cell suspension of bone marrow of a non-irradiated donor into irradiated animals (28, 47-51,61, 64, 65, 93-98, 100-105, 118-121, and others). With a dose of radiation producing the death of 100 percent of the irradiated animals, the intravenous administration of bone marrow for the first four hours after the irradiation increased the survival rate to 75-90 percent

These investigations posed the problem of the nature of the protective factor in hematopoietic tissue (5). Certain authors believe that the protective effect of this tissue in radiation sickness is associated with the influence of acellular humoral factor. Ellinger (58, 59), who has been able to reduce considerably the mortality rate of irradiated mice by means of an intramuscular injection of sterile acellular extract of a homologous spleen of non-irradiated mice, particularly defends this point of view.

However, in recent years a progressively greater number of works has appeared in which the problem of the protective factor in hematopoietic tissue is regarded in a different light. In 1954, Lorenz and Congdon (94) found that death of mice from radiation sickness can be prevented by the administration not only of homologous but also of heterologous (from guinea pigs) bone marrow. The same results were obtained by Jacobson, Marks, and Gaston (83) through the injection of a suspension of mouse spleen cells into irradiated animals. These data were first considered a confirmation of a humoral theory, because the heterotransplants of the hematopoietic tissue usually do not "take" in the recipient organism.

Further investigations made it possible to establish the fact that both in experiments with iso- and homotransplantation and in experiments with heterotransplantation of hematopoietic tissues the protective effect can be produced by the multiplication of the administered cells in the organism of the irradiated recipient.

How can we establish the fact of the multiplication of cells of administered hematopoietic tissue in the bodies of irradiated animals? The solution of this problem would be based on the development of a method which would make it possible to show the multiplication of donor cells in the recipient organism, which would make it possible to identify these cells.

Investigations accomplished in this direction have led to the developme of four methods of identifying foreign cells of hematopoietic tissue in the bodie of irradiated animals: histochemical, cytological, immunological and physico-chemical. These methods have made it possible to detect donor cells in the recipient organism not only from heteroplastic but also from homoplastic transplantations of hematopoietic tissue.

1. The histochemical method is a very demonstrative one, making it possible to detect the existence and multiplication of granulocytes of rats in the bodies of mice. This method is based on the fact that granulocytes of rats contain considerably more alkaline phosphatase than similar mouse cells (142).

2. The cytological method, proposed by Ford and co-workers (62-64), makes it possible to identify donor cells in the recipient organism in experimen of homotransplantation of hematopoietic tissue into mice. The authors made use

of T-6 mouse strains for this purpose in which one of the two chromosomes is always smaller than its paired chromosome during metaphase and has a characteristic shape. After administering splenic cells of a mouse of this strain into irradiated mice of another strain these small marker chromosomes could be detected in the recipients in all cases in the dividing cells of the bone marrow, spleen, lymph nodes and thymus gland. Trentin (135) in his experiments made use of cytological characteristics of rabbit and guinea pig neutrophils, which have characteristic granules making it possible to distinguish them from mouse neutrophi

3. The immunological method makes it possible to detect donor cells in a recipient organism by means of various immunological reactions. Thus, Makinodan (102) worked out a method making it possible to make a quantitative count of the heterologous erythrocytes in the mouse organism by means of antisera against mouse and rat erythrocytes. Mervin and Congdon (111) showed the existence of bone-marrow cells of mice of another strain in the tissues of irradiated inbred mice; this was determined by the capacity of these tissues for producing a specific transplantation immunity after the injections made into non-irradiated mice of the same strain as the irradiated recipients. A similar principle was utilized in the work of Mitchison (117).

4. The physico-chemical method makes it possible to identify heterologou erythrocytes in the organism of the irradiated recipient. Thus, in the experiments of Makinodan (103) it was possible to distinguish rat erythrocytes from mouse erythrocytes through the physico-chemical characteristics of the rat hemoglobin

in combination with the data of paper electrophoresis.

Therefore, the investigations of recent years have led to the development of methods by means of which it is possible to identify foreign cells in the bodies of irradiated recipients and to establish their percentages with respect to similar host cells, and therefore, to evaluate the degree of "take" of them.

In using these methods, it was possible to show that cells of donor hematopoietic tissue introduced into the irradiated recipients are capable of multiplying in the bodies of the latter.

The best "take" of transplanted hematopoietic tissue in irradiated animals has been observed in isotransplantation experiments. This problem has been studied in greatest detail after the injection of bone marrow cells of non-irradiat mice of the same strain into irradiated mice. Thus, in Trentin's experiments (135, 136) the injection of cells of isologous bone marrow into irradiated mice was accompanied by the prolonged "take" and multiplication of them. Similar results were obtained also by other authors (31, 45, 61). The multiplication and prolonged "take" were observed also after the administration of isologous splenic cells into irradiated animals (117). Mitchison (116, 117) believes that transplanted splenic cells are localized in the strictly homologous tissue of the irradiated recipient, because the transplanted isoantigens were found only in its lymph nodes and spleen.

The prolonged "take" of hematopoietic tissue cells in irradiated recipien was established also in experiments of homotransplantation (62-64, 93, 111, 120, 121, 139). Mervin and Congdon (111) have shown that up to 100 percent of homologo

in the bone marrow of the recipients
cells administered were found in irradiated mice 30 and 60 days/
after treatment
with homologous bone marrow. These cells were found not only in the homologous tissue, as in Mitchison's experiments (117) but also in the lymph nodes and thymus gland.

In the experiments of Odell and co-workers (121) donor erythrocytes appeared in the blood of the recipient (rat) eight days after irradiation and the administration of homologous bone marrow; afterwards, their number increased up to 95 percent of the total number of host erythrocytes.

Therefore, the fact of the successful "take" of administered cells of bone marrow and spleen in experiments of iso- and homotransplantation in irradiated recipients may be considered proved. The injected cells can completely replace the corresponding cells of the irradiated recipient.

The possibility of heterotransplantation of hematopoietic tissue in an irradiated organism is of particular interest. Such a possibility may also be considered proved (51, 65, 66, 102-105, 118, 119, 128, 135, 139, 144, 146). These data have been obtained largely through the injection of rat bone-marrow cell into irradiated mice. Apparently, the effectiveness of transplantation of heterologous hematopoietic tissue depends on the degree of genetic similarity between the donor and the recipient. Thus, in Trentin's experiments (135) the best results after heterotransplantation were obtained from the injection of rat bone marrow into irradiated mice; the poorest results, after the injection of rabbit bone marrow into the same recipients.

The multiplication of cells of rat bone marrow in the bodies of irradiated rats is found as early as five days after the transplantation (118). In Mackinodan's investigation (102) the rat erythrocytes appeared in the blood of the irradiated mice a week after the injection of rat bone marrow, and on the 25th day amounted to about 50 percent of the total number of recipient erythrocytes; in the three surviving mice the rat erythrocytes on the 50th-65th day after irradiation constituted 95-100 percent of the total number of erythrocytes.

In the blood of all the recipients rat granulocytes were found on the 45th-63rd day after irradiation. According to the data of Popp and Smith (122a), the proteins of the rat type were found in the organism of radiation chimaeras even a year after the administration.

The investigations of Gengozian and Makinodan (65) have shown that the effect from the injection of rat bone marrow into irradiated mice can be differen depending on the radiation dose and the quantity of cells injected. With 710 r the injection of these cells caused the death of all the animals, whereas in th controls only 30 percent of the irradiated mice died. With 500 and 600 r the injection of bone marrow also increased the mortality rate by comparison with the control animals. The maximum therapeutic effect of bone marrow was obtained at 950 r. In all the mice surviving more than 150 days and which had been given rat bone marrow following irradiation with 950, 1150 and 1300 r, all the erythrocy were of rat origin. With the same dose of radiation the administration of diffe doses of rat bone marrow exerted different therapeutic effects; specifically, wi

an irradiation of 800 r an injection of 25, 40, 75 and 300x 10^6 cells caused the mortality rate, respectively, of 96, 100, 85 and 60 percent of the animals.

The data presented above permits us to consider/proved the possibility of artificial creation of radiation chimaeras in which the administered foreign hematopoietic tissue is capable not only of multiplying but also of completely replacing the homologous recipient tissue. In connection with this, the problem of the specificity of changes in immunobiological reactions of irradiated animals following the injection of foreign hematopoietic tissue into them is of considera interest.

The research carried out in this direction constitute evidence to the effect that the immunobiological status of radiation chimaeras is changing radica approaching the immunobiological status of the donor. The irradiated animal in which the administered foreign hematopoietic tissue has replaced a large part or all of the homologous host cells begins to react to the injection of different antigens, not as a recipient but rather as a donor.

This altered reactivity is manifested particularly in a change in t reaction of irradiated recipients to a skin transplant or transplant of other tissue from various strains of animals which were utilized as hematopoietic tis donors. The homo- and heterologous chimaeras acquire a tolerance to the skin transplant taken from the donor of the same species or strain the hematopoietic tissue of which had been injected after irradiation (101, 135, 136, 147). The state of tolerance to the skin transplants, that is, the lack of the ability to

slough them off, has proved to be strictly specific (101).

A study of this phenomenon in heterologous chimaeras is of particular interest. In the experiments of Zaalberg, Vos and van Bekkum (146), mice which had been exposed to X-irradiation with 675 and 800 r were protected with bone marrow of rats of the Wistar strain.

Pieces of skin of rats of the same strain were transplanted into 35 surviving mice 24-151 days after irradiation of the recipients. The normal growth of the transplant was noted in 10 mice in which all the granulocytes and erythrocyt were of rat origin. In nine animals the growth of the transplant was disturbed; in these mice, the populations of rat and mouse erythrocytes and granulocytes in the blood were mixed. In three animals sloughing-off of the transplant was observed with the absence of rat cells in the peripheral blood. The remaining 13 mice died whereby in all cases the transplants were viable at the time of death. In the control experiments after the transplantation of rat skin into 37 non-irradiated mice the transplant was sloughed off in all the recipients 12 days after grafting.

The altered reactivity of the radiation chimaeras is manifested also in their capacity of elaborating proteins, the antigenic characteristics of which are identical with the characteristics of the hematopoietic tissue donor proteins (47, 144). Thus, in Congdon's experiments (47) the irradiated mice which were given rat bone marrow began to elaborate rat gamma-globulins.

The natural immunity of the radiation chimaeras also changes with respect to the pathogenic microorganisms, acquiring features characteristic

of the immunobiological status of the hematopoietic tissue donor (131). Such deep-seated changes in the immunobiological characteristics of radiation chimaeras most frequently develop as a result of the administration of foreign bone marrow into irradiated recipients. This makes it possible to suppose that the capacity for elaborating a transplantation immunity, like the synthesis of serum gamma-globulins, is associated, to a considerable degree, with the activity of bone-marrow cells, or that other cellular elements capable of producing various immunobiological reactions of the organism are produced from these cells.

Experiments in treating radiation sickness by means of hematopoietic tissue have shown that with the administration of homo- and heterologous hematopoietic tissue into irradiated animals, despite the "take" of the injected cells and a distinct reduction in the mortality rate of the irradiated recipients during the first 20 days after irradiation, part of the animals die at later periods (after 21-120 days). This so-called "secondary disease", producing the late death of irradiated animals is not observed after isotransplantation.

Immunobiological mechanisms underlie the "secondary disease". After the isotransplantation of bone-marrow cells or spleen no cases of late death are noted within the limits of the same strain in irradiated animals, because there are no distinct immunological incongruences between the recipient and the donor. In the experiments of homo- and heterotransplantation this incongruence is expressed to quite a marked degree, as a result of which the "secondary disease" occurs.

Apparently, the late mortality rate of radiation chimaeras is the result of an antigen-antibody reaction (31, 65, 81, 104, 127, 129, 134, 135, 137-139). This point of view may be considered generally accepted. However, in the matter of the mechanism of this reaction there are three different viewpoints. Some investigators believe that antibodies are elaborated by the organism of the irradiated recipient following the recovery of the immune system of the host whic had been injured as the result of irradiation (65, 104); it is believed that these antibodies occur because of the reaction of the recipient to antigens of the injected hematopoietic tissue with which they afterwards combine producing the "secondary disease". Other research workers believe that the injected hematopoietic elements, multiplying and substituting for the hematopoietic tissue of the irradiated recipient and its immune system themselves elaborate antibodies directed against the host tissues (31, 129, 134, 137, 138). A third viewpoint amounts to the assumption that, depending on specific conditions, both of these possibilities may occur (81, 127, 139).

Each of these hypotheses is based on definite experimental proof. Th the fact that the late mortality is observed from the 21st through the 60th day after irradiation, when the mechanism of antibody production in the irradiated donor has recovered to a considerable degree, speaks on behalf of the first hypothesis. Here, all the foreign cells are not necessarily destroyed the animal may die much sooner. In addition, it should be kept in mind that a marked depression of antibody formation in acute radiation sickness is noted

chiefly after the injection of non-living antigens; after the injection of live cells (microbes) the depression of antibody production is expressed to a weak degree and only under certain conditions (29). Makinodan (104) believes that if a transplanted hematopoietic tissue elaborates antibodies directed against the host tissues the globulin of the same antigenic type as that of the transplant should be found in the organism of the host. However, Makinodan did not find such proteins in the recipient organism. This viewpoint is confirmed also by the fact that, first of all, the immune reaction in irradiated recipients does not depend on the dose of bone marrow administered (65, 104) and decreases with the increase in the radiation dose from 710 to 1150 r (65, 104); secondly, with the increase in the radiation dose the immune reaction and the late mortality occur later (104), which is hard to explain from the reaction of the transplant to the host.

The hypothesis which regards the "secondary disease" as a result of the reaction of transplant to the host tissues also has a very definite experimental basis. First of all, if cells of an isologous spleen or thymus gland are injected into irradiated animals simultaneously with the injection of heterologous bone mar several hours after the irradiation the early sloughing-off of the foreign bone marrow and the absence of its therapeutic effect are noted (127); an injection of isologous lymph node cells along with the foreign bone marrow into irradiated recipients, just as in the case of protection of the spleen with lead, causes the death of 100 percent of the animals from a lethal dose of radiation, despite the

injectio.. of bone marrow (81). This may be explained by the fact that the uninjured lymphoid cells of the donor following irradiation elaborate antibodies against the cells of foreign bone marrow entering the irradiated organism. In other words, in these experiments the elaboration of antibodies is accomplished apparently by the lymphoid tissue transplant rather than by the organism in which the corresponding cells have been injured by radiation; the injection of liver cells incapable of forming antibodies does not exert any such effect.

Secondly, F_1 hybrids are better bone marrow donors than mice of the same strain as the host (81, 137), producing almost three times as great a survival rate in the irradiated animals. This phenomenon may be explained only by the characteristics of the reaction of the injected hematopoietic tissue of F_1 hybrids which do not react to the host tissues, because it contains their antigeni components.

Thirdly, the injection of embryonic hematopoietic tissues in radiation sickness exerts a better therapeutic effect than the injection of hematopoietic tissues of adult organisms (17, 81, 137). This may be explained by the fact tha the embryonic tissues are immature in an immunological sense and cannot react immunologically to the host tissues; as a result, the"secondary disease" does not occur or is expressed weakly.

It should be also kept in mind that the death of homo- and heterologous chimaeras can occur as a result of the depletion of the donor lymphoid tissue by the host antigens (31),or an immunological paralysis (60) of the

transplanted cells may be manifested which is accompanied by the recovery of the chimaeras.

Therefore, both hypotheses are reinforced by definite data. Therefore, the third viewpoint is not surprising, according to which both possibilities are very real, but the degree of expression of each of them depends on the specific conditions in each case. The mechanism of the "secondary disease" depends on a quantity of uninjured immunogenetic host tissue remaining after the irradiation as well as the degree of regeneration of it (127). If, for example, the irradiated host is capable of sloughing off foreign hematopoietic tissue and, at the same time, survives, it therefore possesses an adequately functioning hematopoietic tissue, either its own or administered isologous tissue.

For the purpose of understanding the "secondary disease" and the late mortality of radiation chimaeras the adaptation process between the l organism and the foreign tissue injected (81) should be kept in mind. The donor cells may exist in a genetically different host only if such a mutual adaptation of host and donor tissues has occurred that they have stopped reacting against one another. This state of tolerance can be developed in the event the maturation of immunogenetic host or donor tissue is accomplished in the presence of corresponding foreign antigens. In radiation chimaeras the recovery of the host tissue from the effect of radiation develops in the presence of the hematopoietic donor tissue; on the other hand, in the event of repopulation of the donor cells i an irradiated organism these multiplying cells can also adapt to antigens of the host

and
tissues become tolerant with respect to them.

In the case of an incomplete adaptation or an absence of it a "secondary disease" develops, which occurs apparently as a result of a chronic antigen-antibody reaction. If the adaptation is complete, the "secondary disease" does not develop, and late death is not observed. The degree of this adaptation depends on a number of conditions and chiefly on the radiation dose, the quantity of foreign hematopoietic tissue and the method of its administration, the time of the injection, etc. However, in the final analysis, this process depends on the interaction of two factors: the degree of regeneration of the immunogenetic tissue of the irradiated recipient and the degree of repopulation of the immunogenetically active cells of the administered hematopoietic donor tissue.

We have given our principal attention to the transplantation of hematopoietic tissue in irradiated animals, because specifically in these experiments the most interesting results have been obtained. However, the application of ionizing radiation gave investigators new experimental opportunities for the transplantation of other tissues also.

One of these fields of application of ionizing radiation is the so-called "adaptive immunity", that is, immunity which develops after passive transfer of cells of the immunized donor into the non-immune receipient.

At the present time, the possibility of a passive transference of an increased sensitivity to tuberculin and other substances as a result of the injectio of lymphocyte suspensions or suspensions of other cellular elements from

animals infected with tuberculosis to tuberculin-negative recipients of the same species may be considered proved (69, 87, 88, 112, 113, 143). It has also been established that cells of the immunized donor can synthesize antibodies in the organism of a new host (23, 56, 70, 72-77, 125, 126, 130, 132) when injected into a non-immune recipient of the same species, that is in homotransplantation experiments.

Further investigations have shown that the preliminary irradiation of the recipient contributes to a more successful transference of the capacity of elaborating antibodies by donor cells in the organism of the new host (56, 70, 72, 77, 125).

Harris and Harris (72) have established the fact that a total-body X-irradiation of rabbits with 425 r a day before they have been injected with a suspension of cells of regional lymph nodes of an immunized donor prevents the process of active immunization, but at the same time contributes to the accumulation of antibodies in the bodies of the recipients; in these experiments, the cells of the lymph glands of the donor functioned for six to seven days in the organism of the irradiated recipient.

In the experiments of Harris and co-workers (74), in rabbits which had been irradiated with 425 r a day before the injection of cells of regional lymph nodes of a rabbit donor into them, which latter had been immunized with dysentery bacteria, agglutinins appeared in the same way as in the irradiated recipients, that is, on the first day after transplantation, but in a higher titer, and remained and were maintained at this high level for a longer time. Irradiation of the recipients an hour after the injection of donor cells produced a reduction in the antibody titer by comparison with the non-irradiated

control; with irradiation a day after the transfer this difference was reduced, and with irradiation two days after the transplantation the antibody titer was the same in the irradiated and non-irradiated recipients. The authors explained this by the fact that with the increase in the lapse of time between the irradiation and the injection of the lymphoid cells the depressive effect of radiation on these cells is reduced, because afterwards they come from the blood into the organs, which possibly reduces their radiosensitivity. With the injection of lymph node cells into irradiated rabbits after their incubation with antigenic material in vitro agglutinins appear in the recipients on the fourth day after the transfer, and then increase in titer and, finally, their titer begins to increase in the same sequence as after the transference of the cells taken from the immunized donors (77).

Therefore, preliminary irradiation of recipients in doses produci a depression of antibody formation does not prevent, but rather in a number of ca contributes to the functioning of donor cells in the recipient organism, wherein the latter are capable of synthesizing antibodies. However, it should be noted that a temporary "take" of the donor cells, which form antibodies in the organism of radiated and non-irradiated recipients is possible only after iso- and homotransplantation and is not possible with heterotransplantation (36, 73, 133). At the same time, with the direct effect on donor cells in vitro the ionizing radiation completely suppresses the process of antibody synthesis by the given ce These investigations are of great importance for clarifying the mechanism of antibody synthesis. It should, however, be kept in mind that preliminary irradiation of t recipient in various cases may produce a depression of adaptive immunity (55).

At the present time, it may be considered proved that ionizing radiation reduces the natural immunity to transplants of various normal and tumor tissues. Irradiation of the recipients contributes, particularly, to a longer survival of the skin homotransplant (1, 2, 17, 71, 100). A reduction of the protective properties of irradiated organisms against the tumor transplants (99) as well as against the homotransplant of an ovary in mice (122) and against a liver homotransplant of newborn rabbits (123) has also been determined. However, it is essential to take into consideration the fact that a depression of transplantation immunity under the influence of irradiation is by far not always observed (17, 55), whereby the degree of this depression can be very slig (122). In any case, it should be emphasized that suppression of transplantation immunity in irradiated animals with respect to the hematopoietic tissue is expres incomparably more distinctly and in more regular fashion than is observed with respect to other animal tissues.

At the present time, the use of hematopoietic tissue for the treatm of radiation sickness is complicated by the fact that in the administration of homo- and heterologous bone marrow (or spleen) a considerable portion of the irradiated recipients dies on the 21st-120th day after irradiation because of "secondary disease". Therefore, the most important problem in this field is the development of methods of prophylaxis of the late mortality in homologous and in heterologous radiation chimaeras. In this direction certain encouraging results have already been obtained. Thus, for example, A. Lengerova (17, 92) established the fact that after the administration of homologous embryonic cells of hematopoie tissue "the secondary disease" and the late mortality are not observed. Similar results have been obtained by Uphoff (137). This gives us the basis for hoping

in the near future effective agents will be found for combating "secondary disease" which will make it possible to use a suspension of cells of homologous and heterologous hematopoietic tissue for the treatment of radiation sickness.

In March 1959 the works of Jammet, Mathé and others (85) were publi in which the results of are presented of the successful application of homologous bone marrow emulsions for the treatment of radiation sickness in persons suffer because of an accident in a nuclear reactor in Yugoslavia 15 October 1958. At th time of publication of the article all four patients were in satisfactory conditi However, the authors do not exclude the possibility of secondary immunological reactions later.

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